

The menopause: stressors and facilitators

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Between about ages 40 and 55 years, women experience a transition known as the menopause, which marks the end of their childbearing years. Although the most striking feature of the menopause is the cessation of menstruation, other biologic and psychosocial events occur and can be classified as stressors and "facilitators". For a predisposed group of women the stressors are likely to cause psychiatric disorders. At the same time, the facilitators are opportunities for personal growth and development. Physicians who understand both types of events during this phase of life and who are sensitive to the overall effects of ageing on marital partners can provide comprehensive care to the menopausal patient rather than automatically pursuing drug therapy (substitution hormonal therapy) alone.

Entre l'âge de 40 et 55 ans environ, les femmes vivent une période de transition appelée ménopause marquant la fin des années de fertilité. L'événement le plus apparent de la ménopause est la fin des menstruations, mais d'autres événements biologiques et psychosociaux se produisent et jouent un rôle d'agents catalyseurs ou de facteurs de stress. Pour

certaines femmes susceptibles, les facteurs de stress peuvent provoquer des problèmes psychiatriques. Les catalyseurs, par contre, peuvent contribuer à la croissance et au développement personnel. Les médecins qui comprennent les deux genres d'événements que peut comporter cette période de la vie et qui sont conscients des effets généraux du vieillissement sur le couple peuvent soigner de façon compréhensive la femme ménopausée, plutôt que de se contenter de donner un traitement aux médicaments (hormonothérapie substitutive).

The relationship between hormone levels and psychosocial changes during the menopause is not clear: the latter have been studied only in the past 20 years. Stressors contribute to biologic and psychosocial dysfunction during this phase but may be offset by "facilitators", events that offer opportunities not only for women undergoing the menopause but also for the physicians who are called upon to provide care.

Evaluation of the biologic and psychosocial changes during the menopause has been hampered by the lack of standard definitions. One international attempt to define terms differentiates between the climacterium and menopausal phases.¹ The climacterium is seen as the period from about ages 40 to 55 years when a woman passes from the reproductive to the nonreproductive stage. This period is subdivided into the premenopause, in which the menstrual cycle is likely to be irregular, the menopause, which is the time of the final menstruation, and the postmenopause, which is marked by involution of the ovaries. Most studies to date have not differentiated between these terms. Our review,

therefore, uses the widespread term "menopause" as synonymous with "climacterium".

The menopause and psychiatric symptoms

Past reviews and comparisons have been unable to find a specific constellation of psychiatric symptoms that characterizes the menopause,²⁻⁴ perhaps because the symptoms have not been systematically studied. Reports have been limited to the patients' descriptions and have not included objective checks or controls for bias in symptom reporting.

Although depressive disorders, particularly mild ones, are treated twice as often in women as in men, they do not correlate with the menopause.^{5,6} According to an urban survey, however, major depression tends to occur most often at ages 46 to 65 years, when the discrepancy between the sex-specific incidence rates is low.⁷ In patients predisposed to depressive episodes Winokur⁸ showed that the incidence of depressive illness was not greater during the menopause than at other times, nor was the menopause associated with an increase in the incidence of depressive psychosis or suicide.⁹ So far there is no evidence that the menopause is directly associated with a specific psychiatric diagnostic entity.

Stressors related to the menopause

Biologic

Various endocrine dysfunctions have been observed in patients with affective disorders, including women in the menopausal age group.^{10,11} Some of the abnormalities, such as

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decreased levels of growth and luteinizing hormones and varied prolactin levels, may be due to primary hypothalamic or pituitary dysfunction rather than to fluctuations in the endocrine function of peripheral organs.¹²⁻¹⁵ In a well controlled study depressed men and depressed menopausal women showed a normal response of the hypothalamic-pituitary-gonadal axis to the infusion of gonadotropin releasing hormone.¹⁶ The same infusion in postmenopausal women aged 46 to 64 who had primary endogenous unipolar depression with no physical or laboratory abnormality produced levels of luteinizing hormone about 33% below those of healthy postmenopausal controls with no history of personal or family psychiatric illness. The researchers hypothesized that, rather than having a pituitary abnormality, the patients had no internal feedback to the hypothalamus to increase the output of gonadotropin releasing hormone.

However, the major hormonal change — the decrease in estrogen levels — has not been clearly linked with emotional problems. Likewise, catecholamines and estrogen interact, but the exact mechanism and its effects on psychological symptoms are also uncertain.¹⁷⁻¹⁹

Clearly, biologic changes do affect women's sexual desire. In a study of 50 couples, among whom all the women were postmenopausal, the most common problems were loss of orgasm, dyspareunia and secondary erectile difficulty. Of the 50 women, 14 had experienced changes in sensitivity to touch that ranged from hyperirritability to numbness. Interestingly, estrogen has been shown to affect neural transmission time.²⁰ Estrogen therapy will offset these biologic effects but does not address the interpersonal problems and sociocultural values that may be the psychosocial stressors.

Psychosocial

Neugarten and colleagues²¹ found that increased age and experience with menopause significantly improved women's ability to cope with the transition: younger women held more negative and undifferentiated attitudes than did their older counterparts.

In the 1940s Deutsch²² wrote of the menopause as "a narcissistic mortification" by which a woman "loses all she received during puberty". More recent literature, such as Parlee's work,²³ acknowledges that women cannot be seen solely in terms of their reproductive cycle. The biologic changes are often only as important as they are perceived to be within the particular sociocultural environment. A transcultural survey found that women who want to produce more children have a negative attitude toward the menopause.² Among the Fulani in Sudan the menopause is virtually social death, as a woman gives away the last of her calabashes and cattle to her children and goes to live with her eldest son.²⁴

The menopause is part of the much larger process of ageing, and attitudes toward the two overlap. The decline in physical and intellectual abilities associated with ageing is especially difficult for people to accept in societies that value youthful appearance and attractiveness more than experience.²⁵ The menopause is often regarded as a milestone on the road to death, a reminder of human vulnerability.²⁶

Ageing, like the phenomena of the menopause, is accompanied by role changes that are related not only to oneself but also to one's spouse, parents and children. Women must adjust to giving up the maternal role, and the loss is particularly complicated and stressful if the children have become maladjusted adults. Those women who have totally devoted themselves to the raising of children are likely to harbour feelings of guilt and failure if the children do not turn out as expected.²⁵

When children are grown and married or otherwise out of the home, both parents may experience feelings of disinvestment in the "empty nest", and these feelings may lead the partners to withdraw or withhold support for each other's developmental challenges.

Changes in sexual performance can be the source of psychological stress for both partners. Interpersonal issues and sociocultural values can create barriers that underline the biologic effects. Men may experience physical difficulties with pen-

etration, slowness of sexual response and various inhibiting emotions, such as fear of hurting, feelings of rejection or inadequacy, and anger.²⁰

Societal expectations for women reaching their middle years during the 1980s contrast sharply with those in the recent past and may lead to stress. The earlier caricature of a married, obese, idle, depressed woman — the traditional myth²⁷ — is impossible to reconcile with the current picture of a middle-aged woman exploring new careers, heading back to school for a master's degree or striking out on a path for independence, competence and personal growth. A woman may end up feeling she must choose between doing "nothing" at home or doing "everything".

The psychosocial stressors are numerous, and, despite the evidence against psychiatric illness specific to the menopause, many women seek help for complaints of a psychiatric nature in conjunction with the menopause. Thus, physicians need a thorough understanding of the "facilitators" that can offset some of the stressors.

"Facilitators" in the menopause

The restrictive concepts of loss and stagnation associated with the menopause are being increasingly challenged, and many studies are now focusing on the opportunities emerging during this phase of life. Developmental life phases for women no longer correlate with age, as they did in the past: social and biologic cycles for women do not necessarily coincide.²⁸

According to Erikson's model of personality development,²⁹ generativity, defined as a new commitment to guiding younger generations, is the midlife task. According to this model, in midlife individuals shift from pouring all their energies into their advancement and begin caring for others in the broadest sense. This may apply more to men than women in the sense that many women have already invested in this type of generativity in raising their children. During the menopause creativity in one's own activities may be an added dimension for the already generative spouse and mother. Women may start a career as their

children become independent, thus entering the phase of career consolidation a decade or so after men.

The menopause can mean increased freedom, a fact that is clear in several sociocultural environments. For the Rajput woman in India the end of the reproductive cycle means that she becomes freer within her own household, can visit other households and for the first time is allowed to talk and joke with men.²⁴ Also, women of oriental background have been shown to welcome the end of childbearing.²

The "empty-nest syndrome" as a menopausal stressor has been increasingly challenged. Women who maintain a good relationship with their children and those whose identity is less child-centred do not feel threatened by the launching of their children into the adult world. Marital satisfaction may actually increase as stressful postadolescent children leave home.

With fewer time-consuming family responsibilities, women can set other priorities. Interestingly, this life phase parallels adolescence in its potential, although it offers fewer choices and a more limited time frame. The limitations may be offset by the woman's added experience and her understanding of the choices.

The new freedom extends to women's access to health services. The "change of life" is a socially sanctioned reason for women to apply for help, perhaps long needed and neglected. During the menopause a particularly high proportion of women seek professional services. Kessler and colleagues,³⁰ reviewing the evidence from four large-scale surveys of community health, concluded that, compared with men, women more readily translate non-specific feelings of distress into the conscious recognition that they have an emotional problem.

Nevertheless, many do not recognize their problem. Munro³¹ found that 10% of first attenders at a gynecologic outpatient clinic were psychiatrically unwell. This group was particularly likely to complain about menorrhagia and postmenopausal bleeding. Likewise, Ballinger,³² studying psychiatric morbidity in clinic attenders and in the general population, suggested that

patients with depressive illness in particular have a preoccupation with physical symptoms and that these patients may be a vulnerable group with a pattern of experiencing psychiatric symptoms in relation to stressors, of which the menopause is one. Many other factors, such as dysmenorrhea, limited education, sexual or marital problems, and negative sociocultural perceptions have been reported to identify this group; however, the techniques of sampling and analysis have varied widely.²

Further study of the attributes of women in whom psychiatric symptoms develop during the menopause and of their management is needed. At present the evidence for the importance of social and psychologic factors in the genesis of psychiatric disorders during the menopause is stronger than is that for biologic factors.

Unfortunately, cultural attitudes, especially sex-role stereotypes, may influence the quality of mental health services and can create barriers to the delivery of care to women.³³

Clinical observations

Although the bulk of the literature fails to support the traditional concept of a single, universally experienced clinical syndrome during the menopause, there is evidence that some women experience psychiatric morbidity in an incompletely defined relationship to the menopause.^{2,3,6,8,18,31,32,34-36} Physicians who become involved in the assessment and treatment of such women must be able to view the menopause as an occurrence shared by many women working through mid-life tasks. They must develop an understanding of the issues that become important during this phase of life. The approach to treatment is more complex than simply rectifying a hormonal deficiency. Our experience at St. Boniface General Hospital has convinced us that one needs to take a comprehensive biologic and psychosocial approach to treatment, as in the following case.

A 56-year-old married woman related that she had never felt happy in her life but had been feeling progressively sadder, more anxious and more hopeless for 5 years. She had been amenorrheic for 3 years

and had experienced vasomotor symptoms for 2 years despite a prescription for medroxyprogesterone acetate (Provera). For several months she had experienced insomnia and had wakened during the night drenched with perspiration.

She related her sadness to life-long feelings of inadequacy. As a child she had been given no praise and was constantly criticized by her mother, a trend continuing to the present. As a woman she had been unable to conceive. As a mother she perceived antisocial and schizoid traits in her adopted children. She had spent the last 2 years worrying about the impending retirement of her husband, a diabetic sales representative whom she described as a workaholic. She noted sadly that most of her friends, and even her 74-year-old mother, worked full time, yet she resisted her own urge to work outside the home.

Underneath her passive dependency was a great deal of anger toward those to whom she felt inferior, notably her mother and her husband. Her husband consistently denied any ailment, a reaction that did not help the therapy. Over the course of 15 months, individual therapy with an "authority figure" was characterized by mere ventilation of frustration, whereas in a group focusing on assertiveness she was able to express her resentment more constructively. Just before she joined the group her complaints about vasomotor symptoms increased, and the gynecologist treating her prescribed conjugated estrogens (Premarin). She experienced some relief from these symptoms but was unable to dispel the feelings of loneliness and anxiety. Her participation in the group, however, allowed her to rehearse a new, more independent family role. She is now involved in volunteer work and is looking forward to more time for herself. Her symptoms have markedly abated, and her need for hormonal substitutes has decreased.

Management

The first step in the treatment of the patient we have described was individual assessment and therapy, so that the stressors and facilitators could be thoroughly explored. In view of the vulnerability of patients

with long-standing maladaptive personality disorders, this step is an important one.³²⁻³⁴ We recommended assessment of marital communication for the spouse, but he was unwilling to participate. His denial of his own ailments enhanced his wife's guilt for "giving up" to her symptoms. Step two was analysis of the progress made in therapy. In this particular case, group therapy emerged as the best environment for treatment, as it brings together people with diverse backgrounds, education and personality but with common features related to developmental stage, frustrations and anger. A group therapy program involving 10 sessions with both educative and interactive components has been initiated in our clinic. Self-help groups, now found in many towns, focus on the challenges of the middle years, including the menopause, and can also be used as a resource by physicians.

Despite our recommendations a significant proportion of patients' spouses are unwilling to participate in counselling. Sheehy³⁷ described the different directions that men and women may take during the middle years, the "age 40 crucible": "While some women will pause and try to rebalance whatever distortions they feel between personal contentment and worldly aspirations. . . men . . . run harder in an even narrower track!" For some men, conformity to corporate achievement may lead to the perception that work performance is the only criterion of self-worth. They may also feel compelled to ignore all physical reminders of their advancing age. The mounting strong-mindedness of the wife and the increased emotional vulnerability of the husband may lead to a struggle and an upset in the balance of intimacy. The husband may envy his wife because she has found freedom while he has narrowed his horizons.

Although hormonal replacement therapy reduces the menopausal symptoms of vasomotor instability and atrophy of the genital mucosa and may also retard osteoporosis, there is little evidence to support its use as a primary treatment of psychological problems in the menopause.³⁸ Estrogen replacement has been promoted as having secondary

psychologic benefits, as it improves a patient's feelings of physical well-being, but this idea is controversial.^{18,38} The advantages of estrogen replacement therapy must be carefully weighed against the disadvantages, which include an increased risk of cancer of the endometrium.

Voda³⁹ has concluded that if women had definitive data about the temporal aspects of the menopause, and particularly the vasomotor symptoms, they would be much better able to cope without estrogens. The conclusion arose from a study into the strategies women use to cope with hot flashes. A sample of 1041 hot flashes, with a mean duration of 3.30 minutes, was obtained for scrutiny by having 20 randomly selected women report daily on their experiences for 2 weeks. The ways that women coped included drinking liquids, standing in front of a source of cool air and showering. Among the activities that triggered the hot flashes, "sleeping, napping and dozing" ranked highest, while "emotions" ranked lowest. (One weakness in the study — and in virtually all similar studies — is the lack of objective measurements of the climacteric symptoms.) Biofeedback has also been suggested as a means to produce relief from hot flashes.⁴⁰

Conclusions

The major feature of the menopause is change. The "change of life" may be of use to women in need of a socially sanctioned reason to go to a physician for help. Research is ongoing in a number of biologic, psychologic and social areas that should help achieve a more precise understanding of the characteristics of the subgroup of women at risk for psychiatric morbidity around the time of the menopause. Because a number of interrelated factors are involved, physicians need to take a comprehensive approach to treatment. Substitution hormonal therapy leads to limited results unless there is also awareness of the psychologic challenges the patient faces and efforts are made to activate her social support network.

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Prescribing Information

Lopresor® (metoprolol tartrate)

50mg and 100mg tablets

200mg slow-release tablets

Therapeutic Classification

Antihypertensive and anti-anginal agent.

Actions

Metoprolol tartrate is a beta-adrenergic-receptor-blocking agent with predominant blocking effect on beta₁ receptors.

Indications

a) Mild and Moderate Hypertension:

Usually used in combination with other drugs, particularly a thiazide diuretic, however, may be tried alone as an initial agent in those patients whose treatment should be started with a beta-blocker rather than a diuretic. The combination of Lopresor with a diuretic or peripheral vasodilator has been found to be compatible and generally more effective than Lopresor alone. Incompatibility with other antihypertensive agents has not been found, experience is limited however. Not recommended for the emergency treatment of hypertensive crises.

b) Angina Pectoris

Lopresor is indicated in patients with angina pectoris due to ischemic heart disease.

Contraindications

Sinus bradycardia, second and third degree A-V block, right ventricular failure secondary to pulmonary hypertension, congestive heart failure, cardiogenic shock, anesthesia with agents that produce myocardial depression, e.g. ether and chloroform.

Warnings

a) **Cardiac Failure:** Special caution should be exercised when administering Lopresor to patients with a history of heart failure, since inhibition with beta-blockade always carries the potential hazard of further depressing myocardial contractility and precipitating cardiac failure. In patients without a history of cardiac failure, continued depression of the myocardium can lead to cardiac failure. At the first sign of impending cardiac failure, patients should be digitalized and/or given a diuretic and observed closely.

Lopresor does not abolish the inotropic action of digitalis on the heart muscle, however, the positive inotropic action of digitalis may be reduced by the negative inotropic effect of Lopresor when the two drugs are used concomitantly. The effects of beta-blockers and digitalis are additive in depressing A-V conduction. If cardiac failure continues, despite adequate digitalisation and diuretic therapy, discontinue Lopresor therapy.

b) **Abrupt Cessation of Therapy with Lopresor:** Warn patients against abrupt discontinuation. There have been reports of severe exacerbation of angina, and of myocardial infarction or ventricular arrhythmias in patients with angina following abrupt discontinuation of beta-blocker therapy. The last two complications may occur with or without preceding exacerbation of angina pectoris. When discontinuation of Lopresor is planned in patients with angina, dosage should be gradually reduced over a period of about two weeks and the patient carefully observed. The same frequency of administration should be maintained. In situations of greater urgency, Lopresor should be discontinued stepwise, under conditions of closer observation. If angina markedly worsens or acute coronary insufficiency develops, it is recommended that treatment with Lopresor be reinstituted promptly, at least temporarily.

c) Various skin rashes and conjunctival xerosis have been reported. A severe syndrome (oculo-muco-cutaneous syndrome) whose signs include conjunctivitis sicca and psoriasisiform rashes, otitis, and sclerosing serositis has occurred with the chronic use of one beta-adrenergic-blocking agent (practolol) but has not been observed with Lopresor or any other such agent. Physicians should be alert to the possibility of such reactions and should discontinue treatment in the event that they occur.

d) Severe sinus bradycardia may occur, in such cases, dosage should be reduced.

e) Lopresor may mask the clinical signs of continuing hyperthyroidism or complications and give a false impression of improvement. Therefore, abrupt withdrawal of Lopresor may be followed by an exacerbation of the symptoms of hyperthyroidism including thyroid storm.

Precautions

a) Careful monitoring of patients with diseases associated with bronchospasm is mandatory and a bronchodilator must be administered concomitantly.

b) Administer with caution to patients subject to spontaneous hypoglycemia or to diabetic patients (especially those with labile diabetes) who are receiving insulin or oral hypoglycemic agents. Beta-adrenergic blockers may mask the premonitory signs and symptoms of acute hypoglycemia.

c) Adjust dosage individually when used concomitantly with other anti-hypertensive agents.

d) Closely monitor patients also receiving catecholamine-depleting drugs, such as reserpine or guanethidine. Lopresor should not be combined with other beta-blockers.

e) Appropriate laboratory tests should be performed at regular intervals during long-term treatment.

f) Lopresor should not be given to patients receiving verapamil. In exceptional cases, when in the opinion of the physician concomitant use is considered essential, such use should be instituted gradually, in a hospital setting, under careful supervision.

g) In patients undergoing elective or emergency surgery: Lopresor should be withdrawn gradually following recommendation given under Abrupt Cessation of Therapy (see WARNINGS). Available evidence suggests that the clinical and pharmacological effects of beta-

blockade induced by Lopresor are no longer present 48 hours after cessation of therapy.

In emergency surgery, effects of Lopresor may be reversed, if necessary, by sufficient doses of such agonists as isoproterenol or levaterenol.

h) **Usage in pregnancy and nursing mothers:** Lopresor crosses the placental barrier and appears in breast milk. It should not be given to pregnant women as it has not been studied in human pregnancy. If use of the drug is deemed essential in nursing mothers, the patient should stop nursing.

i) **Usage in children:** There is no experience with Lopresor in the pediatric age groups.

Adverse reactions

Cardiovascular: Congestive heart failure (see WARNINGS), secondary effects of decreased cardiac output which include: syncope, vertigo, lightheadedness and postural hypotension; severe bradycardia, lengthening of PR interval, second and third degree A-V block, sinus arrest, palpitations, chest pains, cold extremities, Raynaud's phenomenon, claudication, hot flushes.

Central Nervous System: headache, dizziness, insomnia, mental depression, lightheadedness, anxiety, tinnitus, weakness, sedation, vivid dreams, vertigo, paresthesia.

Gastrointestinal: diarrhea, constipation, flatulence, heartburn, nausea and vomiting, abdominal pain, dryness of mouth.

Respiratory: shortness of breath, wheezing, bronchospasm, status asthmaticus.

Allergic/Dermatological (see WARNINGS): exanthema, sweating, pruritus, psoriasisiform rash.

EENT: blurred vision and non-specific visual disturbances, itching eyes.

Miscellaneous: tiredness, weight gain, decrease in libido.

Clinical Laboratory: The following laboratory parameters have been rarely elevated: transaminases, BUN, alkaline phosphatase and bilirubin. Thrombocytopenia and leucopenia have been reported rarely.

Symptoms and Treatment of Overdosage

Symptoms: bradycardia, congestive heart failure, hypotension, bronchospasm, hypoglycemia.

Treatment: Discontinue Lopresor and observe patient closely. In addition, if required, the following therapeutic measures are suggested.

1. Bradycardia, and hypotension:

Initially 1-2 mg of atropine sulfate should be given intravenously. If a satisfactory effect is not achieved, a pressor agent such as norepinephrine may be administered after preceding treatment with atropine.

2. Heart Block: (second or third degree)

Isoproterenol or transvenous cardiac pacemaker.

3. Congestive heart failure:

Conventional therapy.

4. Bronchospasm:

Aminophylline or a beta₂-agonist.

5. Hypoglycemia:

Intravenous glucose.

Large doses of isoproterenol can be expected to reverse many of the effects of excessive doses of Lopresor. However, the complications of excess isoproterenol, e.g. hypotension and tachycardia, should not be overlooked.

Dosage and Administration

a) **Hypertension:** Initial Dose: 50 mg b.i.d. If adequate response is not seen after one week, dosage should be increased to 100 mg b.i.d. In some cases the daily dosage may need to be increased by further 100 mg increments at intervals of not less than two weeks up to a maximum of 200 mg b.i.d., which should not be exceeded.

Usual Maintenance Dose: 150-300 mg daily. When combined with another antihypertensive agent which is already being administered, Lopresor should be added initially at a dose of 50 mg b.i.d. After 1 or 2 weeks the daily dosage may be increased if required, in increments of 100 mg, at intervals of not less than 2 weeks, until adequate blood pressure control is obtained.

b) **Angina pectoris:** Initial Dose: 50 mg b.i.d. for the first week. If response is not adequate, the daily dosage should be increased by 100 mg for the next week. The need for further increases should be closely monitored at weekly intervals and the dosage increased in 100 mg increments to a maximum of 400 mg/day in 2 or 3 divided doses.

Usual Maintenance Dosage: 200 mg/day. Dosage Range: 100-400 mg per day in divided doses. A dose of 400 mg/day should not be exceeded.

c) **Slow-release Lopresor SR 200 mg:** Lopresor SR 200 mg is intended only for maintenance dosing in those patients requiring doses of 200 mg per day. Treatment must always be initiated and individual titration of dosage carried out using the regular tablets. Patients with hypertension or angina pectoris on a maintenance regimen of one 100 mg tablet twice daily may be changed to one Lopresor SR 200 mg tablet in the morning. Lopresor SR 200 mg tablets should be swallowed whole.

Availability

Lopresor

Tablet: 50 mg:

Film coated, light red, capsule-shaped tablet, embossed 51 and scored on one side and GEIGY on the other.

Tablet: 100 mg:

Film coated, light blue, capsule-shaped tablet, embossed 71 and scored on one side and GEIGY on the other.

Lopresor SR

Slow-release Tablet: 200 mg:

Film-coated, light yellow, round tablet, embossed GEIGY on one side and CDC on the other.

Product monograph supplied on request.

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Geigy

Mississauga, Ontario
L5N 2W5